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Facsimile Cover Sheet

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Pages including this cover page: 5

COMMENTS:

RE: SN 09/816,284

I am attaching, as a follow-up to my voicemails of last evening and earlier today, four references that discuss zinc induced anemia and its treatment with copper. I would appreciate the opportunity to discuss the Advisory Action of May 14 in view of these references.

Respectfully submitted,

Denis A. Polyn

Denis Polyn
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1: Sci Total Environ 1985 Mar 15;42(1-2):37-43 elated Articles in

Copper responsive anemia, induced by oral zinc therapy in a patient with acrodermatitis enteropathica.

Hoogenraad TU, Dekker AW, van den Hamer CJ.

Normocytic anemia with granulocytopenia occurred in a 23 year old man with acrodermatitis enteropathica who received high doses of zinc sulphate orally for 12 months. Copper deficiency was suspected to be the cause of this anemia when extreme hypocupremia and hypoceruloplasminemia wer found. Oral zinc therapy was stopped and intravenous supplements of copper were followed by reticulocytosis and complete correction of the anemia and granulocytopenia. Plasma copper and ceruloplasmin levels normalized. Up to now copper deficiency has never been reported during zinc treatment in acrodermatitis enteropathica. We conclude that the coppe status should be monitored during oral zinc therapy in this condition.

PMID: 4012288 [PubMed - indexed for MEDLINE]

1: Am J Dis Child 1992 Jun;146(6):709-11

Zinc-induced copper deficiency in an infant.

Botash AS, Nasca J, Dubowy R, Weinberger HL, Oliphant M.

Department of Pediatrics, State University of New York Health Science Center, NY 13210.

OBJECTIVE--To describe the case of a 13-month-old girl who developed copper deficiency as a result of excessive zinc gluconate ingestion. SETTING--Tertiary care hospital in Syracuse, NY. INTERVENTIONS--Cessation of zinc ingection followed by intravenous and oral copper chloride therapy. MEASUREMENTS/MAIN RESULTS--Ingestion of zinc gluconate, 120 mg/d for 6 months, and thereafter 180 mg/d for 1 month, preceded the clinical presentation of listlessness, anemia, neutropenia, poor weight gain, abnormal sparse hair, and scorbuticlike bone changes. Findings on a bone marrow examination included ring sideroblasts and suggested copper deficiency. Plasma zinc level was 36.7 mumol/L, serum ceruloplasmin level was 20 mg/L, and serum copper level was undetectable. Clinical and laboratory abnormalities resolved shortly after initiation of copper therapy. CONCLUSIONS--This case demonstrates the reciprocal relationship of copper and zinc metabolism and exemplifies the important interrelationships of dietary trace minerals.

PMID: 1595625 [PubMed - indexed for MEDLINE]

1: Gastroenterology 1988 Feb;94(2):508-12

Gastroenterology

Zinc-induced copper deficiency.

Hoffman HN 2nd, Phyliky RL, Fleming CR.

Department of Internal Medicine, Mayo Clinic, Rochester, Minnesota.

Copper deficiency was found in an adult patient who had received excessive daily oral zinc for 10 mo. The deficiency was characterized by hypochromic-microcytic anemia, leukopenia, and neutropenia. Although initially thought to be caused by iron deficiency, the anemia did not respond to oral or intravenous iron. Cessation of zinc tablets and ingestion of an oral copper preparation daily for 2 mo failed to correct the anemia or leukopenia. It was not until shortly after intravenous administration of a cupric chloride solution during a 5-day period, at a total dose of 10 mg, that serum copper and ceruloplasmin levels increased and the anemia, leukopenia, and neutropenia resolved. These data suggest that the elimination of excess zinc is slow and that, until such elimination occurs, the intestinal absorption of copper is blocked.

PMID: 3335323 [PubMed - indexed for MEDLINE]

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1: JAMA 1978 Nov 10;240(20):2166-8

Hypocupremia induced by zinc therapy in adults.

Prasad AS, Brewer GJ, Schoomaker EB, Rabbani P.

Hypocupremia occurred in an adult with sickle cell anemia who received zinc as an antisickling agent for two years. The hypocupremia was associated with microcytosis and relative neutropenia. Administration of copper resulted in an increase in RBC size and leukocyte counts. We have since observed hypoceruloplasminemia of varying degrees in several other sickle cell anemia patients who were receiving oral zinc therapy. This complication was easily corrected by copper supplementation.

Publication Types:
Clinical Trial

PMID: 359844 [PubMed - indexed for MEDLINE]